REMARKS

Applicants express their appreciation for the consideration extended by the Examiner and her supervisor in the interview conducted on June 24, 2010 (hereinafter "the Interview"). The following Remarks are submitted in response to the concerns expressed by the Office during that interview.

Response to Interview Summary

During the course of the interview, the Office requested clarification regarding where support for certain amendments is found in Applicants' specification. Applicants note that a copy of the published PCT application was submitted to the Office on December 3, 1999, which document is present on PAIR under Document Code 371P. A specification was also filed on December 3, 1999, which document is present on PAIR under Document Code SPEC. The electronic document viewed by the Examiner and her supervisor during the course of the interview corresponds to Document Code SPEC. For the convenience of the Office, Applicants have re-framed the response filed on May 5, 2010 to refer to the page numbering present in Document Code SPEC and to address the concerns expressed by the Office during the Interview.

The question of whether identity and homology are equivalent terms was raised during the interview. This issue is moot given that the specification as filed provides support for 95% identity at page 8, lines 11-15.

During the interview, the Examiner also asked whether Applicants had disclosed polypeptides that were at least 95% identical. As indicated during the interview, Applicants' specification describes a number of polypeptides having various degrees of identity to SEQ ID NO:2, including RP-factors of *M. tuberculosis* and *M. luteus*. Although *M. luteus* and *M. tuberculosis* share less than 95% identity as shown in Figure 1A, both proteins share similar cell growth promoting activity (page 48, line 24-page 49, line 21, page 52, line 6, to page 53, line 11, page 57, line 16, to page 59, line 19). In view of this finding, one of skill in the art would expect that proteins having a higher degree of identity to SEQ ID NO:2 would also promote the growth of dormant cells. Moreover, once provided with SEQ ID NO:2, one of skill in the art could readily identify proteins having at least 95% identity to that sequence.

Once the Examiner has had an opportunity to consider the re-framed response below, Applicants' respectfully request that the Examiner contact Applicants' representative to schedule a follow-up interview with the Examiner and her supervisor.

Objection to the Specification

In the Office action and in the Interview, the Examiner objected to Applicants' specification based on the assertion that Applicants' specification fails to provide support for polypeptides having 95% identity to SEQ ID NO. 2. Applicants respectfully disagree.

Applicants' specification is not limited to the purified RP factors described in the Examples. Applicants' specification clearly describes the use of polypeptides having at least 95% identity to RP factor (SEQ ID NO:2). More specifically, at page 8, lines 11-15, Applicants' specification states:

> Particularly preferred are homologues, derivatives, muteins or equivalents of the RP-factor of the invention which have at least 30% identity, for example at least 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 98% identity with any one of the particular amino acid sequences shown in Fig. 1A or Fig. 1B (emphasis added).

Clearly, Applicants specification provides support for proteins having at least 95% identity. Applicants also provide at Figure 1 an alignment of proteins having various degrees of identity with SEQ ID NO:2. In view of this disclosure, Applicants' specification clearly encompasses the use of RP-factors having at least 95% identity to SEQ ID No. 2. Therefore, this objection to the specification should be withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

The rejection of claim 159 as allegedly indefinite is rendered moot by the cancellation of the claim.

The rejection of claims 128, 144, and 158 is overcome by the present amendment.

Rejections under 35 U.S.C. § 112, first paragraph

New Matter

Claims 126-128, 131, 144, 148-150, and 157-159 are rejected under 35 U.S.C. § 112, first paragraph as allegedly including new matter that was not described in the application as filed. In support of the rejection, the Examiner asserts that the specification fails to provide support for polypeptides having at least 95% sequence identity to SEQ ID NO:2 or to amino acids 117-184 of SEQ ID NO:2. This is incorrect.

As discussed above, Figure 1A provides the sequence of a number of RP factors, including SEQ ID NO:2 and the asterisks in Figure 1A identify amino acids 117-184 of SEQ ID NO:2. Moreover, Applicants' specification describes such sequences at page 8, lines 11-15:

> Particularly preferred are homologues, derivatives, muteins or equivalents of the RP-factor of the invention which have at least 30% identity, for example at least 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or 98% identity with any one of the particular amino acid sequences shown in Fig. 1A or Fig. 1B (emphasis added).

In view of this disclosure, the new matter rejection is improper and should be withdrawn.

Written Description

Claims 126-128, 131, 144, 148-150, and 157-159 are further rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking a written description. In support of the rejection, the Examiner indicates that Applicants have not described a sufficient number of polypeptide variants to establish how sequence changes would affect the function of the protein. Applicants respectfully disagree.

An adequate written description of the invention may be shown by any description of sufficient, relevant, identifying characteristics so long as a person skilled in the art would recognize that the Applicants had possession of the claimed invention (M.P.E.P. 2163.04 II.A.3(a)). Applicants' specification clearly satisfies the written description requirement. Using sequence information relating to *M. luteus* RP-factor, Applicants have identified RP factor

proteins from other bacteria, including SEQ ID NO:2 from *M. tuberculosis*, that share sequence identity with *M. luteus* RP-factor (page 50, line 9, to page 51, line 6, under the header "Identification of RP-factor homologues"). Applicants have used the sequence information obtained from *M. luteus* to identify related RP-factors in a number of other organisms, including *M. tuberculosis*, *M. leprae*, *Streptomyces rimosus*, *M. smegmatis*, *M. bovis*, and *Corynebacterium glutamicum* (page 50, lines 22-25, and page 51, lines 2-6).

Applicants have provided an alignment of RP factor proteins in Figure 1A, which identifies conserved structural features and highly conserved amino acid residues (page 51, line 7 to page 52, line 2, under the heading "Domain structure"; Figures 9A and 9B). Applicants found that RP-factors share a secretory signal sequence and a conserved 70-residue segment that may act as a signaling domain (page 51, lines 10-12). This domain includes four conserved tryptophan residues and two conserved cysteine residues that may form a disulfide bridge (page 51, lines 27-28 and page 52, lines 1 and 2). These structural features are conserved among a wide variety of proteins and are, therefore, likely to be functionally important. In view of this disclosure, Applicants' specification clearly provides guidance relating to those regions of the protein where sequence variations are likely to be tolerated and those conserved regions where variations in the sequence are less desirable (See also, page 10, line 11, to page 17, line 10).

Moreover, one of skill in the art could readily identify those variant polypeptides that fall within the scope of Applicants' claims (i.e., those polypeptides having at least 95% amino acid sequence identity to SEQ ID NO:2 that are capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell) using routine methods that are described in Applicants' specification. For example, Applicants' specification clearly describes methods of screening for polypeptides capable of resuscitating dormant bacteria using purified RP-factors (page 48, line 24, to page 49, line 21, and page 52-53, under the heading "RP Factor Activity"). Such screening could easily be accomplished using standard techniques that are plainly described in Applicants' specification.

In particular, Applicants expressed a secreted form of the *M. tuberculosis* polypeptide in *E. coli* (page 54, line 4, to page 57, line 27). This fragment of SEQ ID NO:2 included amino acids beginning at D50 of the amino acid sequence, and included amino acids 117-184 as recited

in the claims (page 57, lines 16-25)). The purified protein was added to cultures of *M. luteus* and *M. tuberculosis*. Applicants found that as expected SEQ ID NO:2 stimulated the growth of *M. tuberculosis* cells and *M. luteus* cells (page 57, line 16-line 27). Applicants found that the control culture grew to a final OD_{600nm} of 1.0 (page 57, lines 25-27). In contrast, cultures treated with purified RP-factor continued to grow to final OD_{600nm} of 2.0-6.0 (page 57, lines 25-27). These results indicated that a SEQ ID NO:2 polypeptide containing amino acids 117-184 was capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell under conditions where the control culture failed to grow.

In sum, Applicants have described a number of polypeptide variants, have described a correlation between structure and function, and have described methods for identifying polypeptides having the desired biological activity. This description clearly establishes that Applicants had possession of the invention as claimed. Accordingly, the written description rejection should be withdrawn.

New Claims

Applicants have added new claims 160-164, which are directed to methods for resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells that feature the use of a polypeptide comprising SEQ ID NO: 2 or comprising at least amino acid residues 117 to 184 of SEQ ID NO: 2. In particular, claims 160 and 161 are directed to methods of resuscitating a dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cell by contacting the *Mycobacterium tuberculosis* bacterial cell *in vitro* with a purified polypeptide comprising SEQ ID NO:2 (claim 160) or a purified polypeptide comprising at least amino acid residues 117 to 184 of SEQ ID NO: 2 (claim 161), where the polypeptide is capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell; and incubating the bacterial cells in culture medium containing the polypeptide, thereby resuscitating said bacterial cells. Claim 162 depends from claims 160 and 161.

Claims 163 and 164 are directed to methods of resuscitating dormant, moribund or latent *Mycobacterium tuberculosis* bacterial cells by contacting the bacterial cells *in vitro* with a cell strain expressing a nucleic acid encoding a polypeptide comprising SEQ ID NO: 2 (claim 163) or encoding at least amino acid residues 117 to 184 of SEQ ID NO: 2, where the polypeptide is

capable of resuscitating a dormant, moribund, or latent *Mycobacterium tuberculosis* cell; and incubating the cells and cell strain in culture medium, thereby resuscitating the cells.

Applicants believe that these claims are commensurate in scope with the subject matter that the Examiner has indicated is allowable. Accordingly, allowance of claims 160-164 is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe the pending application as amended herein is in condition for allowance. Therefore, Applicants respectfully request entry of the amendments and remarks presented herein, favorable reconsideration and withdrawal of all pending rejections, and issuance of a Notice of Allowance. However, if the Examiner disagrees and a telephone conference would be helpful to expedite further prosecution and allowance of this application, Applicants respectfully request the Examiner to contact the undersigned at the telephone number indicated below.

Dated: July 13, 2010

Respectfully submitted,
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